Profile

Paul Nurse: cycling up the hill

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Combining primary research with the administrative demands of a senior position in science is a tricky balancing act. But Paul Nurse, who has recently been appointed Director General of the UK's prestigious research organization, the Imperial Cancer Research Fund (ICRF), certainly has no intention of retiring behind a desk. His promotion from Director of Laboratory Research promises to bring exciting times to the ICRF. With his background in the fundamental research that has revolutionized our understanding of the cell cycle, and his commitment to continuing his primary research, Nurse will be directing the ICRF into the next century clutching a petri dish in one hand.

Nurse was brought up in a North London working-class household and was the only one of four children to carry on education beyond school. After completing secondary education, he worked for a year in the Guinness Brewery laboratories, where he was first introduced to large-scale screening procedures. This consolidated his interest in biology, which he went on to study at Birmingham University. After graduating with Honours, he moved to the University of East Anglia for his doctorate, to study the intracellular localization of molecules during cell division. A large part of this work involved baby-sitting a temperamental amino-acid analyzer, which often required attention into the small hours of the night. During one of these nocturnal vigils, he recalls reading a paper by Lee Hartwell describing how genetics could be used to study the cell cycle in budding yeast. Nurse was inspired by the elegant use of genetics to study a fundamental process and wanted to try a similar approach in fission yeast. But there were a couple of problems: he knew not a great deal about yeast and even less about genetics.

Nurse contacted Murdoch Mitchison, a prominent fission yeast physiologist in Edinburgh, who agreed that this was a very exciting approach but one that would require Nurse to learn some yeast genetics. Nurse was given funding for six months from the Royal Society to learn these techniques from Urs Leupold in Bern, Switzerland. In 1974, Nurse joined Mitchison's lab and began screening for mutated yeast strains that divided abnormally. The first mutant was soon identified and isolated on the basis of its small size during cell division (with a dash of his infamous humour, he wanted to christen it *wee1*, 'wee' being Scots for tiny). Nurse continued to expand his collection of mutant strains and used genetic techniques to identify the network of genes controlling the fission yeast cell cycle. Mitchison's lab soon became a meeting point for other cell cyclers, such as Kim Nasmyth, who did his doctoral research with Nurse, and Peter Fantes and Pierre Thuriaux, who were interested in the regulation of cell-size control.

In the late 1970s, techniques were developed for transforming budding yeast with exogenous DNA. Unfortunately, this technology — which would have allowed Nurse to isolate the actual genes mutated in his yeast strains — was not available for fission yeast. Never one to fight shy of a problem, Nurse moved to the University of Sussex to establish methods for transforming fission yeast. This was a long and arduous task but, with the help of David Beach, he got the technique working and used it to isolate the *cdc2* gene from one of his strains.

In 1984, Nurse joined the ICRF laboratories in London. Although the ICRF was initially interested in the use of yeast purely as a eukaryotic gene expression system, Nurse soon convinced them of the importance of studies in yeast for understanding the mammalian cell cycle. Using DNA-hybridization techniques, he began hunting for mammalian homologues of his yeast cell-cycle genes, with little success. Nurse recalls thinking it was worth one last shot, and in 1986 he and postdoc Melanie Lee attempted to functionally complement one of their yeast mutants with a library of human cDNAs. Remarkably, it worked, and soon they had isolated the human *cdc2* homologue.

High flyer Paul Nurse, ready for take-off.

Despite his success and the abundant facilities available to him at the ICRF, Nurse took up the post of Iveagh Professor of Microbiology at Oxford in 1987, in a move largely inspired by the better lifestyle Oxford offered his family. His lab grew in size, partly because of an influx of American postdocs attracted by both the excellence of the science and the deserved reputation of 'the wee one' for fairness and frivolity. Then, in 1993, Nurse returned to the ICRF in London as the Director of Laboratory Research. Although taking a position with such heavy administrative responsibilities seemed like a surprising move for a 'hands on' scientist, the organizational structure of the ICRF has allowed him to spend up to half his time in the laboratory. When Nurse moves into the Director-General's chair this month, he will continue to cycle his energies between the lab and the office.